



“Bromination of Acetophenone using *N*-Bromosuccinimide”

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Abstract: Acetophenone react with *N*-bromosuccinimide and *p*-toluenesulphonic acid (*p*-TsOH) using acetonitrile as a solvent to yield α -bromoacetophenone in high yields.

The reaction does not take place in the absence of *p*-

TsOH. However, the reaction is possible photochemically even in the absence of *p*-TsOH.



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Introduction: The α -bromination of carbonyl compounds is an important transformation in synthetic organic chemistry. The α -Bromination of the side chain of aromatic ketones has attracted attention because the resulting bromoketones are intermediates for the synthesis of a variety of biologically active compounds. α -Bromination is the first step of introducing a heteroatom so as to provide additional conjugation to the carbonyl group, and for generating stabilized carbon radicals or carbanions. The reported work on bromination of acetophenones makes the use of bromine and HBr which have several environmental problems. Handling of liquid bromine, due to its hazardous nature is troublesome. In order to overcome these problems, alternative methods avoiding the use of liquid bromine has been developed.

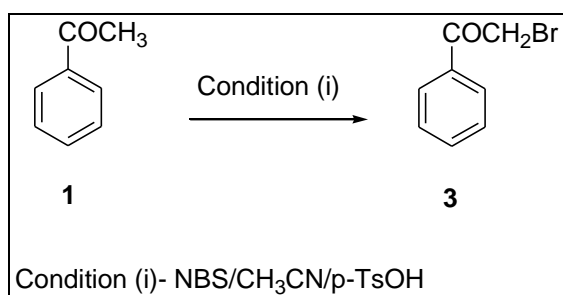
Most recent developments in this area emphasize the advantageous use of NBS over Br₂ under suitable conditions making NBS as a reagent of choice for the following reasons- (i) ease of handling (ii) selectivity of the reaction in appropriate condition (iii) yields of the products (iv) from stand point of green chemistry (v) efficiency of the reaction. As a part of our ongoing programme aimed at the selective bromination of various compounds, we now investigated the bromination of acetophenone using NBS. Consequently, we report herein synthesis of α -bromo derivative of acetophenone.

Result and discussion

Acetophenone was used as a target molecule for study of halogenation using *N*-bromosuccinimide. Bromination with NBS depends on the catalyst used and it has also been confirmed recently that photo initiated transformation in diethyl ether gave a high yield of mono brominated product.



First, we studied the reaction of acetophenone with *N*-bromosuccinimide using acetonitrile as a solvent. The reaction was first observed at room temperature and then under harsh condition. Room temperature reaction was not successful but mixtures of product were obtained under harsh condition (reaction mixture refluxed for long reaction times). Then, reaction was performed using *p*-toluenesulphonic acid (PTSA) as a catalyst. A similar reaction using PTSA gave a much lower conversion after 3h, but could be enhanced by prolonged reaction times and resulted in >75% conversion after 48h.



From the above study, it was concluded that presence of protic acid plays an important role in α -bromination. In order to study the effect of nature of protic acid on the reaction involving use of *N*-bromosuccinimide in acetonitrile, variation of protic acid including trifluoroacetic acid and sulphuric acid has been attempted. The complete results are summarized below:

Table 1. Effect of nature of protic acid on α -bromination of acetophenone

Reaction condition	Time (h)	Yield ^a (%)
NBS/ <i>p</i> -TsOH/CH ₃ CN	12	69
NBS/CF ₃ COOH/CH ₃ CN	14	63
NBS/H ₂ SO ₄ /CH ₃ CN	16	53

^a- yields of isolated products w.r.t NBS

It is clear from the results that the use of protic acids such as *p*-TsOH and TFA gives satisfactory results, whereas in case of H₂SO₄ results are somewhat poorer. Although above method provides a better way for selective α -bromination, there was scope of further improvement of yields.

EXPERIMENTAL



All reagents were purchased from commercial sources and were used without purification. Melting points were taken on slides in an electrical apparatus Labindia visual melting range apparatus and are uncorrected.

To a solution of **1** (10 mmol) and (15 mmol) *p*-toluenesulphonic acid monohydrate in acetonitrile (20ml) was slowly added (11 mmol) NBS in small installment to avoid dibromination. The mixture was stirred for 12 h under reflux. Then the solvent was reduced by distillation to half and cooled down to room temperature and resulting solid was dissolved in dichloromethane, washed with water, and recrystallised using ethanol to gave α -bromo derivative of acetophenone (69%). mp 47⁰C (lit 48-51⁰C)

CONCLUSION

The forgoing results present in this study clearly indicate that NBS mediated bromination of acetophenone offers a far better alternative to the existing methods involving Br₂/HBr. Further the byproduct succinimide can be readily recovered and recycled, thus making the procedure more environmentally acceptable.

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